**Supplemental Digital Content**

**Table e1:** Pump function

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Covariate** | | **Dependent variable** | | **Equation parameters** | | **Difference of slopes** |
|  |  | **rpm**; min-1 | | **QECMO**; mL×min-1 | | **Slope m (95% CI)**  mL × revolution-1 | ***p*** |
|  | n | mean ± SD | range | mean ± SD | range |  |  |  |
| **Euvolemia** | 45 | 2774 ± 782 | 1350 – 4800 | 3069 ± 1083 | 1135 – 5598 | 1.306 (1.024 – 1.588) | ≤0.0005 | n.s. |
| **Vasoconstriction 3** | 2994 ± 808 | 1500 – 5000 | 3381 ± 1179 | 1292 – 6379 | 1.424 (1.327 – 1.521) | ≤0.0005 |
| **Volume Expansion 3** | 3198 ± 864 | 1550 – 5000 | 3971 ± 1328 | 1462 – 7042 | 1.506 (1.391 – 1.620) | ≤0.0005 |

Generalized Estimating Equations. Pump function= ΔQECMO/Δrpm. n=number of data pairs per condition (9 animals × 5 pump speeds). Proportion of variance (Pearson correlation coefficient squared; *r2*) for individual animals (median, range) in Euvolemia: 0.998 (0.844-1.000); Vasoconstriction 3: 0.999 (0.811-1.000); and Volume Expansion 3: 0.999 (0.900-1.000).

|  |  |  |  |
| --- | --- | --- | --- |
| **Table e2:** Baseline comparisons | | | |
|  | **Euvolemia** | **Post Vasoconstriction** | ***p*** |
| MSFP: mmHg | 7.1 ± 1.1 | 6.5 ± 0.7 | 0.227 |
| QECMO; mL×min-1 | 3382 ± 199 | 3144 ± 682 | 0.281 |
| RAP: mmHg | 1.9 ± 2.3 | 1.7 ± 2.7 | 0.881 |
| VRdP: mmHg | 5.1 ± 2 | 4.7 ± 2.8 | 0.773 |
| RVR: mmHg x (mL×min-1) -1 | 1.5 ± 0.6 | 1.6 ± 1 | 0.893 |
| rpm: min-1 | 2978 ± 164 | 2944 ± 403 | 0.733 |

Data are mean ± SD. Paired t-test

**Table e3:** Venous return function – full data set

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Covariate** | | **Dependent variable** | |  | **Equation parameters** | |  |
|  |  | **RAP;** mmHg | | **QECMO;** mL × min-1 | | ***r*2‡** | **Slope (95% CI)**  mL × min-1 × mmHg-1 | **Intercept (95% CI)**  mL × min-1 | *p* |
|  | n | mean ± SD | range | mean ± SD | range | median (range) |  |  |  |
| **Euvolemia** | 54 | 3.6 ± 2.6 | -2.3 – 8.8 | 2558 ±1519 | 0 – 5598 | 0.91 (0.30 – 1.00) | -420 (-545 – -295) | 4053 (3416 – 4689) | ≤0.0005 |
| **Vasoconstriction 1** | 3.2 ± 2.2 | -0.3 – 8.1 | 2534 ± 1500 | 0 – 5483 | 0.87 (0.48 – 1.00) | -620 (-832 – -408)† | 4197 (3292 – 5103) |
| **Vasoconstriction 2** | 4.0 ± 2.3 | 0.0 – 9.5 | 2698 ± 1565 | 0 – 5654 | 0.92 (0.11 – 0.99) | -251 (-390 – -112) | 3969 (3130 – 4808) |
| **Vasoconstriction 3** | 4.4 ± 2.3 | 0.8 – 10.4 | 2817 ± 1665 | 0 – 6379 | 0.80 (0.04 – 1.00) | -295 (-414 – -176) | 4289 (3715 – 4864) |
| **Post Vasoconstriction** | 3.5 ± 2.4 | -2.5 – 7.3 | 2060 ± 1316 | 0 – 4695 | 0.77 (0.13 – 0.99) | -377 (-439 – -315) | 3311 (2793 – 3829) |
| **Volume Expansion 1** | 4.7 ± 2.3 | -0.3 – 13.4 | 2814 ± 1614 | 0 – 5403 | 0.85 (0.10 – 0.99) | -256 (-338 – -174) | 4377 (3991 – 4763)a |
| **Volume Expansion 2** | 5.3 ± 2.1 | 0.3 – 10.5 | 3212 ± 1867 | 0 – 7051 | 0.74 (0.21 – 1.00) | -656 (-811 – -500)\* | 6634 (6095 – 7173)a |
| **Volume Expansion 3** | 5.8 ± 2.0 | 1.5 – 10.9 | 3311 ± 1921 | 0 – 7042 | 0.70 (0.20 – 1.00) | -648 (-773 – -524)\* | 7207 (6302 – 8112)a |

Generalized Estimating Equations for QECMO *vs*. RAP. n=number of data pairs per condition [9 animals × (5 pump speeds + MSFP)]; slope of the line= (resistance to venous return)-1 = (RVR)-1; *p*-value for equation parameters valid for both slopes and intercepts. **‡** Median (range) of proportion of variance (Pearson correlation coefficient squared; *r2*) for individual animals.\*The slopes of Volume Expansion 2 and 3 are significantly different from those of Post Vasoconstriction, Volume Expansion 1, and Vasoconstriction 2. † The slope of Vasoconstriction 1 is significantly different from those of Vasoconstriction 2 and Volume Expansion 1. a The intercepts of Volume Expansion 1-3 were significantly different from that of Post Vasoconstriction.

**Table e4:** Shift in flow at the standardized (averaged) RAP of 2.8 mmHg

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Euvolemia** | **Vasoconstriction** | | | **Post Vasoconstr.** | **Volume Expansion** | | | ***p* values** | | |
|  | Step 1 | Step 2 | Step 3 | Step 1 | Step 2 | Step 3 | treatment | intensity | interaction |
| QECMO: mL/min | 2978 ± 1046 | 2648 ± 636 | 3338 ± 854 | 3529 ± 648 | 2266 ± 856 | 4068 ± 1080 | 5254 ± 1660 | 6196 ± 1788 | 0.01 | <0.0005 | <0.0005 |

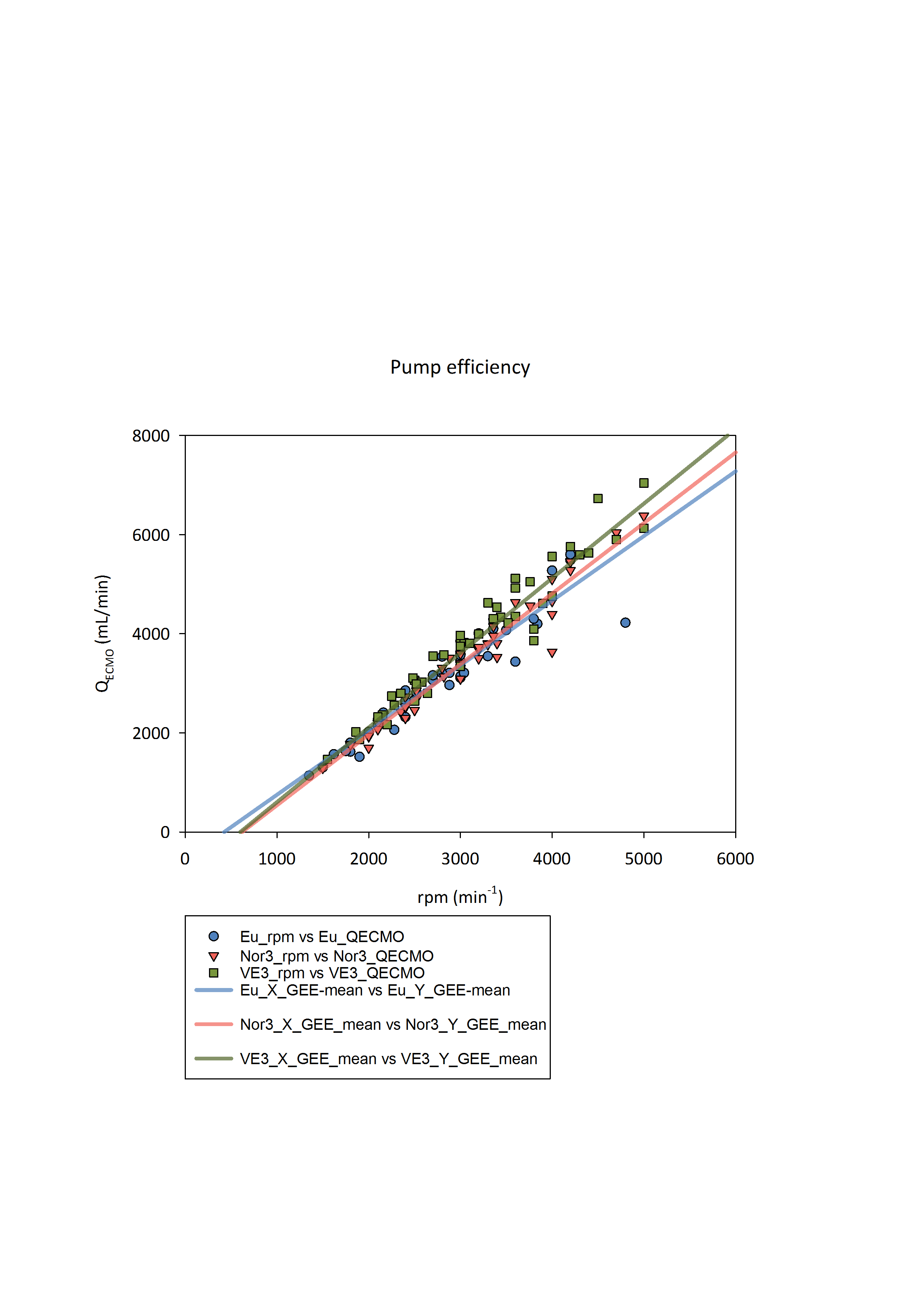
**Table e5**: MSFP decay over time

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | **Covariate** | **Dependent variable**  **MSFP**; mmHg | |  |  |  |  |
|  | | **Time**; min |  |  |  |  |
|  | | range | mean ± SD | range |  |  |  |  |
| **Vasoconstriction 3** | | 0 – 41.6 | 7.39 ± 1.19 | 5.24 – 10.02 |  |  |  |  |
| **Volume Expansion 3** | | 7.82 ± 1.73 | 4.88 – 12.95 |  |  |  |  |
| Total | | 7.56 ± 1.49 | 4.88 – 12.95 |  |  |  |  |
| **Parameter estimates** | | | | | | | | |
| **Intercept** | | | **Slope** | | | **Factor** | | |
| **MSFP**; mmHg | | | **ΔMSFP × time-1**; mmHg × min-1 | | | **Vasoconstriction 3 *vs*. Volume Expansion 3**;  mmHg × min-1 | | |
|  | 95% CI | *p* |  | 95% CI | p |  | 95% CI | *p* |
| 8.74 | 7.95 – 9.54 | < 0.0005 | -0.043 | -0.065 – -0.021 | < 0.0005 | -0.50 | -1.21 – 0.02 | 0.173 |

Generalized Estimating Equation. n=9. Dependent variable: MSFP (mmHg). Covariate: time (as continous variable). Factor: Vasoconstriction 3 *vs*. Volume Expansion 3. In the above model, the interaction term condition × time was excluded: it was not significant and resulted in worse model fit.

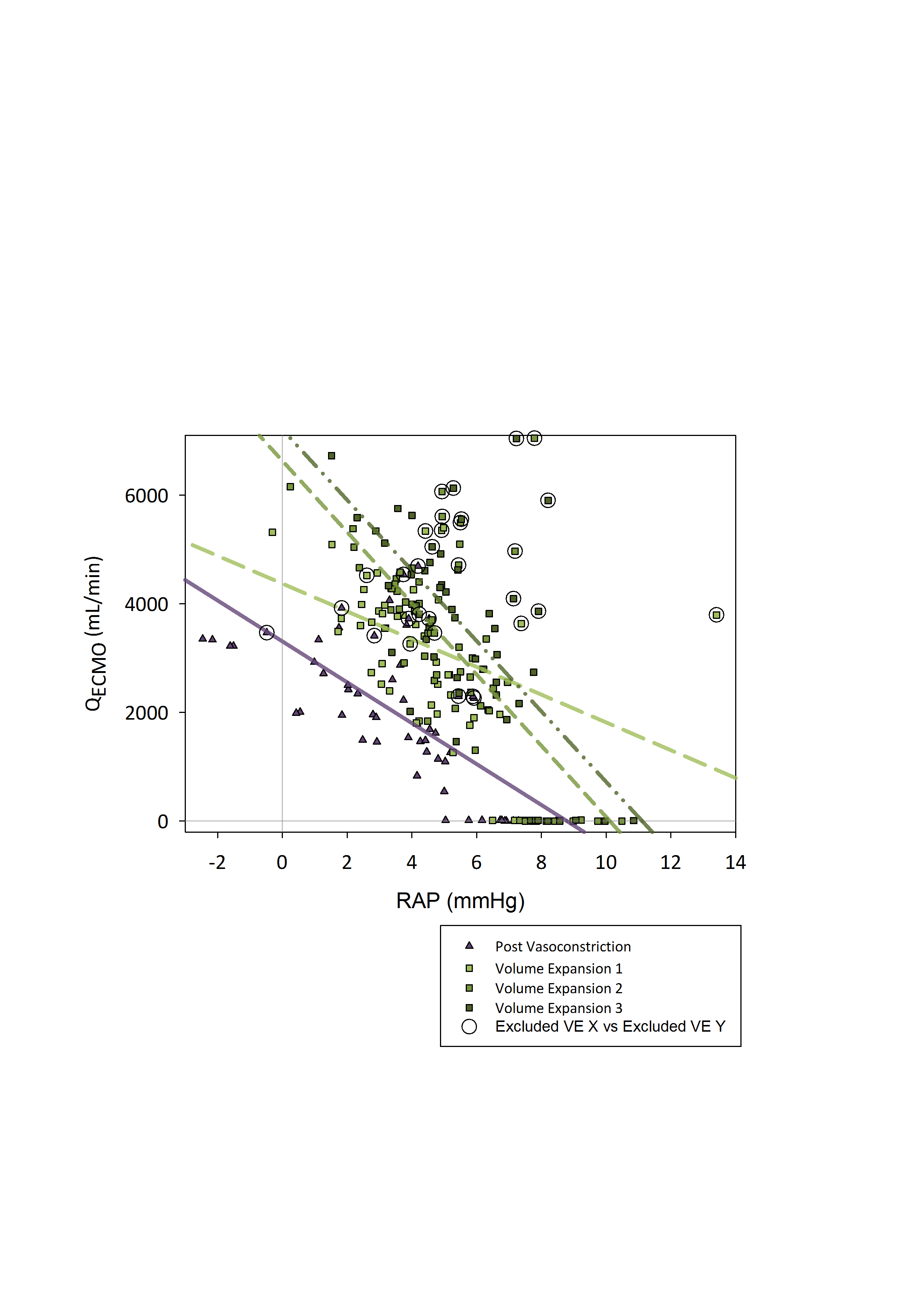
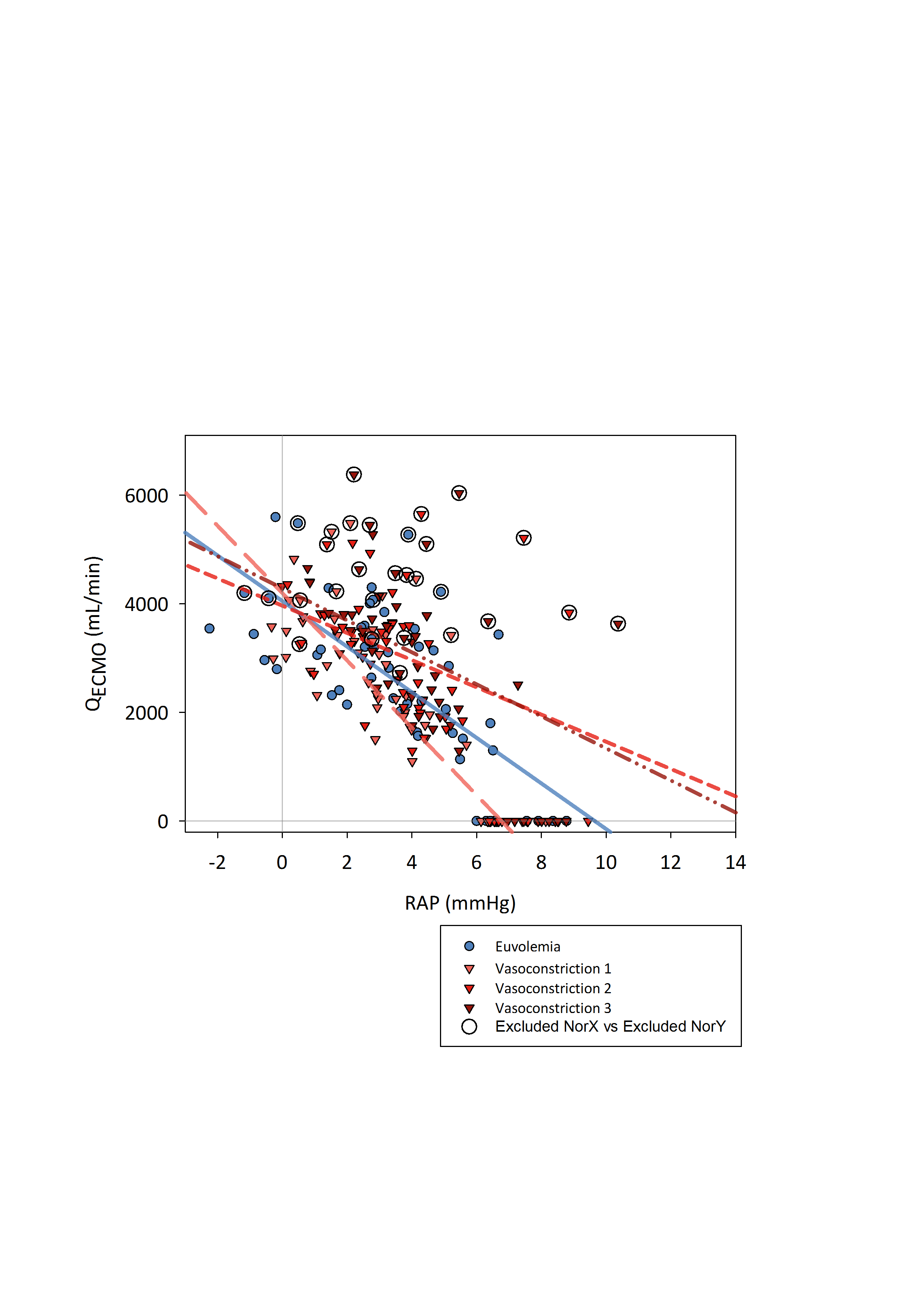
**Figure e1:** Scatter plot of QECMO *vs*. rpm data-pairs with mean slopes of GEE.

Equation details are found in supplemental Table e1.

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**Figure e2**: Venous return curves for the full data set

Equation details are found in supplemental Table e3



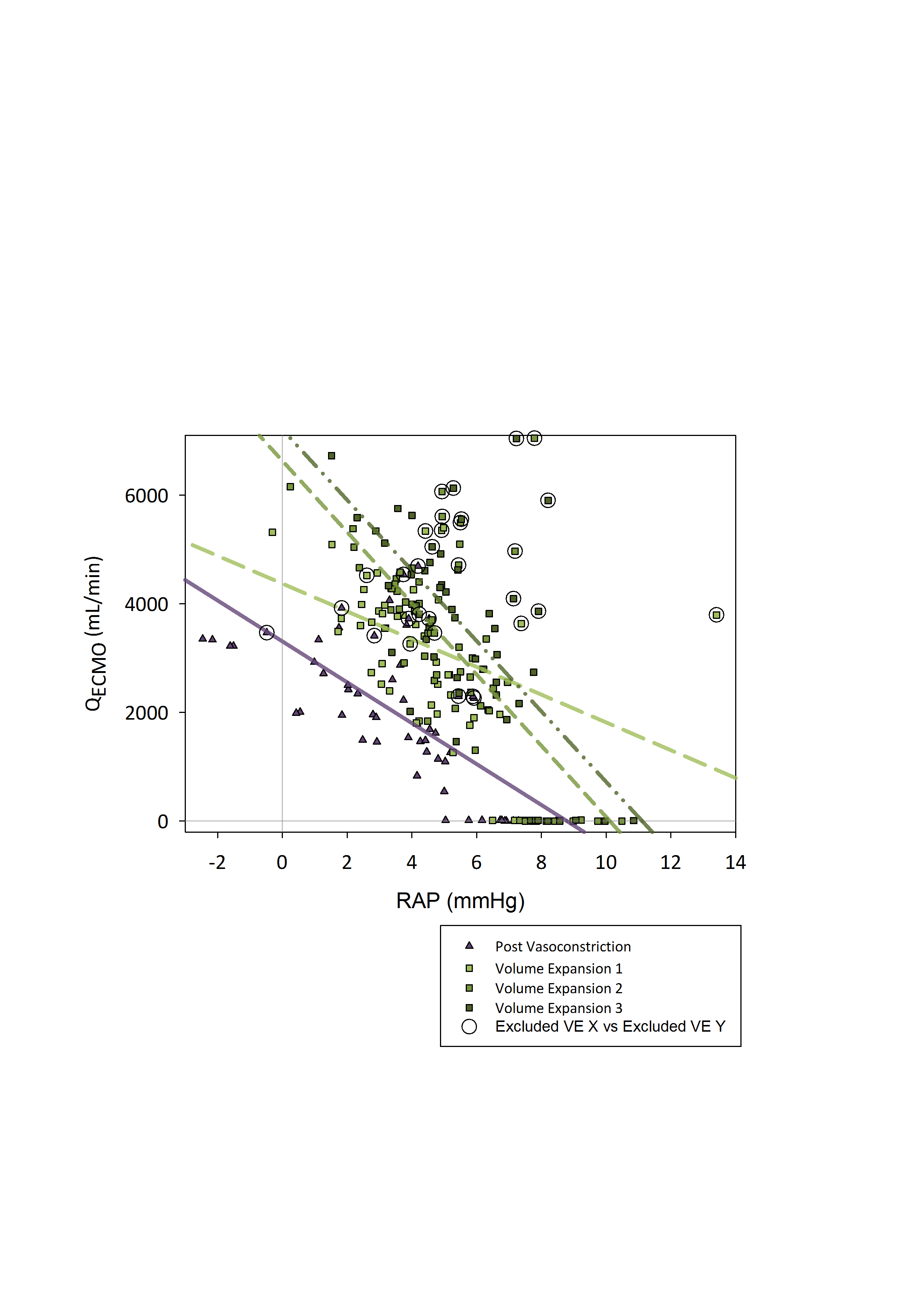
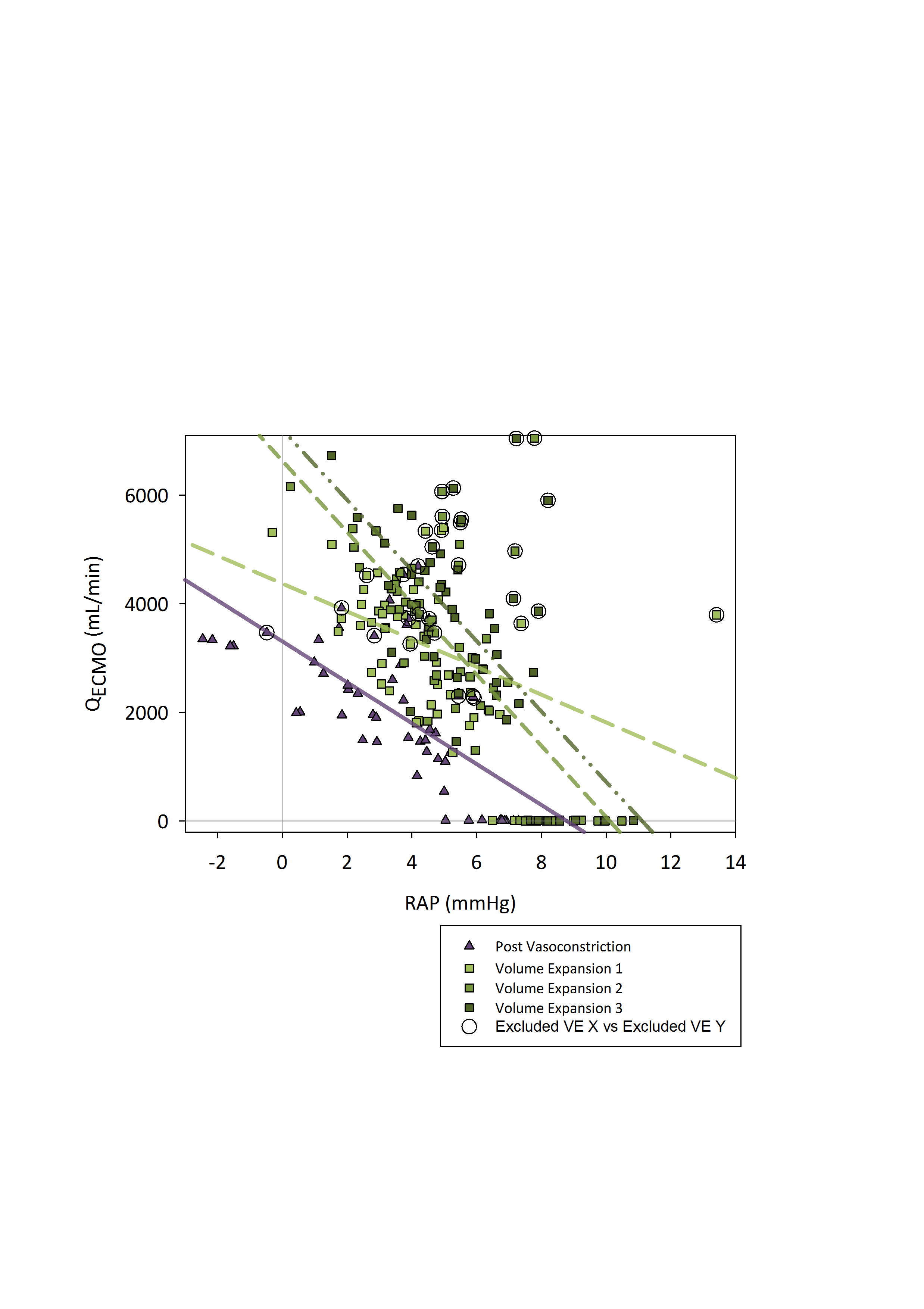
Euvolemia

Vasoconstriction 1

Closing conditions

Vasoconstriction 2

Vasoconstriction 3



Post Vasoconstriction

Volume Expansion 1

Closing conditions

Volume Expansion 2

Volume Expansion 3

